Center for Medical Countermeasures Against Radiation

DAIT Regulatory Affairs

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Clinical Research Programs

- Immune Tolerance Network (ITN)
- Cooperative Clinical Trials in Pediatric Transplantation (CCTPT)
- Clinical Trials in Organ Transplant (CTOT)
- Hematopoietic Stem Cell Transplantation (HSCT)
- Autoimmunity Centers of Excellence (ACE)
- Inner-City Asthma Consortium (ICAC)
- Atopic Dermatitis Vaccinia Network (ADVN)
- Islet Cell Network
- Center for Medical Countermeasures Against Radiation

Collaborative Effort

- DAIT, NIAID, NIH
- NCI, NIH
- FDA Division of Counterterrorism
- CDER/FDA
- CBER/FDA
- DHHS
- DHS
- Others

Regulatory Affairs

- **DAIT Staff**
- **Contract Research Organization (CRO)**
- **Individual Consultants**
  - **GLP toxicology**
  - **GMP quality**
  - **GMP facilities**

Drug Development & Approval Process

	Pre-clinical testing			Phase I	Phase II		Phase III				FDA	Approval
Year	1	2	File IND	3	4	5	6	7	8	File NDA or BLA	9	10
Test population	Laboratory & Animal Studies			20 to 80 patient volunteers	100 to 300 patient volunteers		1,000 to 3,000 patient volunteers				Review usually takes about 2-3 years	Post-marketing safety monitoring Large-scale manufacturing Distribution Education
Purpose	Assess safety and biological activity			Determine safety and dosage	Evaluate effectiveness. Look for side effects.		Verify effectiveness, monitor adverse reactions from long-term use.					
					Expedited Review: Phases II and III combined to shorten approval process on new medicines for serious and life-threatening diseases.							

Applicable Regulatory Tools/Strategies

- **Fast Track Designation**
- **Priority review**
- **Subpart H (Accelerated approval using a surrogate endpoint)**
- **Subpart I (the “Animal Efficacy Rule”)**
- **Orphan Drug Designation**
- **Special FDA Programs (e.g. FDA Division of Counter-terrorism - Liaison)**

The “Animal Rule”

Approval of Biological Products (New Drugs) when Human Efficacy Studies are Not Ethical or Feasible

- **Final Rule:**
  - 67 FR 37988 (May 31, 2002)
  - 21 CFR § 601.90-95 (biologicals)
  - 21 CFR § 314.600-650 (drugs)

Scope of the "Animal Rule"

- **Drugs and biologicals that reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances.**

- **Rule does *not* apply if product approval can be based on standards described elsewhere in FDA's regulations.**

FDA may approve a product for which...

- **Human safety has been established,**

  and

- **"Animal Rule" requirements are met – based on adequate and well-controlled animal studies, the results of which establish that the products is reasonably likely to provide clinical benefit in humans.**

GLP & AWA Requirements

- **All studies subject to this Rule must be conducted in accordance with preexisting requirements under the Good Laboratory Practices (21 CFR §58) regulations and the Animal Welfare Act (7 U.S.C. 2131).**

- **GLP will be required for the definitive/pivotal animal studies – not necessary for the pilot studies. Also, if the animal study will be mentioned in the label, it should be done according to GLP.**

Animal Study Design Challenges

- **The label indication.**
  - **Pre-exposure/post exposure.**
- **Endpoints of animal studies.**
  - **IACUC and EU regs.**
- **Appropriate challenge dose.**
- **Statistical considerations.**
  - **Rodents vs. NHP**

Conclusions

- **The “Animal Rule” is new to both industry and to the FDA – collaboration is essential for success.**
- **Multiple interactions with FDA**
  - **prior to animal efficacy trials, for concurrence with concepts.**

Information Resources

- **FDA Website**
  - **http://www.fda.gov**
- **Small Business Assistance**
  - **http://www.fda.gov/cder/about/smallbiz/default.htm**

Information Resources

- **IND Regulations: Code of Federal Regulations, Title 21, parts 312 and 50.**
- **ICH E6 Good Clinical Practice: Consolidated Guidance**
  - **www.fda.gov/cder/guidance/959fnl.pdf**
- **Formal Meetings with Sponsors and Applicants for PDUFA Products**
  - **www.fda.gov/cder/guidance/2125fnl.pdf**

Contact Information

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